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Journal
Journal of Stroke and Cerebrovascular Diseases, 22(7)

ISSN
1052-3057

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Publication Date
2013-10-01

DOI
10.1016/j.jstrokecerebrovasdis.2012.05.004

Peer reviewed

Published in final edited form as:
J Stroke Cerebrovasc Dis. 2013 October ; 22(7): 1038–1045. doi:10.1016/j.jstrokecerebrovasdis.2012.05.004.

Impact of Gender and Blood Pressure on Post-Stroke Cognitive Decline among Older Latinos

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Abstract

Background—Post-stroke cognitive decline (PSCD) is an important consequence of stroke that may be more severe in women than men. The existence of any gender differences in PSCD among

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Author Disclosures
Dr. Deborah A. Levine reports research support from the NIH (P30 AG024824-07 [sub-project PI]).
Dr. Mary N. Haan has held funding from NIH grants AG12975, AG 033751 and DK60753.
Dr. Kenneth M. Langa reports research support from the NIH (R01 AG030155 [Co-Investigator]).
Dr. Lewis B. Morgenstern reports research support from NIH grants NS062675 and NS038916.
Dr. Morgenstern is on the Editorial Board of *Stroke*.
Dr. John Neuhaus is a statistical editor of *Archives of Internal Medicine*, Associate Editor of *Biometrics*, and on the Editorial Boards of *American Industrial Hygiene Association* and *Statistics in Medicine*. Dr. Neuhaus has held funding from NIH grant 5R01CA082370-08.
Anne Lee reports no disclosures.
Dr. Lynda D. Lisabeth reports research support from NIH grants NS038916, HL098065 and NS070941.

Contributions
Dr. Levine - Drafting/revising the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data; study coordination
Dr. Haan – Drafting/revising the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data; acquisition of data; study supervision
Drs. Langa and Morgenstern – Drafting/revising the manuscript for content, including medical writing for content
Dr. Neuhaus and Ms. Lee – Analysis or interpretation of data; statistical analysis
Dr. Lisabeth - Drafting/revising the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data; study supervision

Mexican Americans, and their potential mechanisms, such as blood pressure (BP), remain unknown. We assessed PSCD stratified on gender in older Mexican Americans and explored the influence of pre-stroke and post-stroke systolic BP on PSCD.

Methods—Among 1,576 non-demented, stroke-free adults 60 years or older when recruited in 1998–99 in the Sacramento Area Latino Study on Aging (SALSA) cohort, we examined pre-stroke and post-stroke longitudinal changes in Spanish English Verbal Learning test scores (WL), a verbal memory test, and errors on the Modified Mini Mental State Exam (3MSE) scores, a global cognition test, stratified by gender, adjusting for baseline and time-varying covariates with linear mixed-effects models.

Results—We identified 151 adults (mean age, 72 ± 8 years) with incident first-ever stroke during ten years of follow-up. After adjustment for age, education and time-varying depressive symptoms, 3MSE errors increased by 22%/year (95% CI, 6.8%–36.7%) in men and 13.2%/year (95% CI, 3.5%–22.9%) in women over the post-stroke period. Post-stroke WL scores improved by 0.05 words/year (95% CI, −0.24–0.33) in men and by 0.09 words/year (95% CI, −0.16–0.34) in women. Results persisted after adjustment for time-varying systolic BP.

Conclusions—Among this population of older Mexican Americans, PSCD did not differ by gender. We found no evidence that systolic BP influenced PSCD in women or men.

Keywords

[MeSH] Cerebrovascular disease/stroke; Cognition; Hispanic Americans; Sex; Epidemiology

Introduction

Post-stroke dementia rates are increasing rapidly in older adults,[1] and significant gender disparities in post-stroke dementia may be emerging.[2] Post-stroke cognitive decline (PSCD), both dementia and less severe cognitive impairment without dementia, tends to be higher in women compared with men.[2] However, there is heterogeneity across studies and few studies include Hispanics.[2] Moreover, few studies account for concomitant depression or pre-stroke cognitive impairment, which are known risk factors for PSCD[2–4] that may be more common in women.[5]

Women may have a greater risk of PSCD compared with men for several reasons. Women may have higher levels of PSCD risk factors including older age at stroke onset and lower educational level.[2, 6] Women may have more severe strokes, including cardioembolic strokes, and worse functional recovery after stroke.[7, 8] In addition, women may have a greater burden of underlying cerebrovascular pathology related to a greater degree of white matter lesions[9] or subclinical atherosclerosis.[10]

Hypertension, the most important stroke risk factor, and other stroke risk factors may contribute to gender differences in PSCD.[2] But, whether pre-stroke blood pressure (BP) or post-stroke BP influences PSCD, independent of stroke, is unclear. Moreover, few population-based studies have data to explore whether pre-stroke BP levels influence gender differences in PSCD.[4, 11, 12]

Although Mexican Americans comprise 66% of all Hispanics and have higher stroke incidence rates than whites,[13] little is known about PSCD in Mexican Americans. Mexican Americans represent an ideal group to study the impact of both gender and BP on PSCD. Mexican Americans have a high burden of hypertension but they may have lower treatment and control rates compared to non-Hispanic Blacks and non-Hispanic Whites.[14] Moreover, Mexican Americans have important gender differences in hypertension prevalence, treatment and control. Among Mexican Americans aged 70 years or older, women have higher rates of hypertension prevalence but lower rates of awareness, treatment, and control of hypertension than men.[14] Therefore, we examined PSCD in a longitudinal population-based cohort of older Mexican Americans, before and after stratification by gender, and determined whether systolic BP explains any within-gender differences in PSCD.

Methods

Study Design, Participants, and Measurements

In 1998–1999, the Sacramento Area Latino Study on Aging (SALSA) enrolled 1,789 Latinos (94% Mexican American) aged 60 or older and followed participants through 2008. Participants were randomly selected from specific census tracts of rural and urban areas of Sacramento, California. Participants were recruited using a probability sample taken from census tracts with at least a 5% Hispanic population in a 6-county area. The overall response rate among those contacted was 85%. Annual in-home evaluations included an interview, a medicine chest inventory, a physical exam, blood samples, and cognitive screening tests. All examinations were approved by the institutional review boards of the University of California at San Francisco and Davis and the University of Michigan. Each participant provided written informed consent. Detailed information regarding SALSA methods is available elsewhere.[15]

Of 1,789 SALSA participants, we excluded 168 (9.4%) with stroke at baseline. Of the remaining 1,621 participants, we excluded 45 (2.8%) diagnosed with baseline dementia using a standardized protocol,[15] leaving 1,576 available for analysis.

Outcome Measures

Cognitive testing was performed at each annual follow-up visit. The two primary outcome measures were the Modified Mini-Mental State Examination (3MSE) and the Word-List Delayed Recall trial (WL) of the Spanish and English Verbal Learning Test (SEVLT). The 3MSE is a measure of global cognitive functioning that is strongly associated with dementia.[16] The 3MSE is a 100-point cognitive test with high internal reliability (standardized alpha=0.90), superior sensitivity to the Mini-Mental State Exam, and good sensitivity to change over time.[17] The WL from the SEVLT is a measure of verbal memory and is highly sensitive to cognitive decline.[18] Each test was administered in the primary language (English or Spanish) of the subject or the preferred language of administration of bilingual subjects. All testing was conducted by bilingual/bicultural technicians in the participant's home. English and Spanish versions of SEVLT and 3MSE have been shown to be valid and consistent.[18] The Vascular Cognitive Impairment Harmonization Standards include the WL and 3MSE.[19]

We identified incident strokes using 1) participant self-reports of a physician diagnosis of stroke during the annual in-home examinations or the semi-annual telephone interviews or 2) documentation of stroke as a cause of death on death certificates. For those who reported a stroke and then died of stroke, the date of the stroke report was used in time calculations.

Covariates

Covariates included age[3] based on self-reported date of birth and years of education[3]. Depressive symptoms were measured at each annual follow-up visit using the Center for Epidemiologic Study-Depression (CES-D) scale.[20] At each home visit, after a 5-minute rest, BP was measured in the right arm of seated participants at two 5-minute intervals using an appropriately sized cuff and a standard automated BP measurement monitor (*OmROn* model HEM747IC; Omron, Mannheim, Germany) based on a specific protocol.[21] The BP at each visit in this analysis was the average of the 2 measurements. BP was treated as a continuous variable and time-varying covariate. We focused on systolic BP for several reasons: 1) systolic BP increases with age; 2) elevated systolic BP is the most common form of hypertension in older adults; 3) elevated systolic BP increases cardiovascular risk more than diastolic BP in older patients with hypertension; and 4) elevated systolic BP has been associated with PSCD.[22, 23]

Statistical Analysis

We calculated descriptive statistics such as means and proportions for all study variables, separately by gender. We compared the estimated means and proportions between genders for the entire sample and among those participants who experienced an incident stroke using two sample t-tests or chi-square tests, as appropriate. The analysis sample included participants who did not experience an incident stroke. Time was expressed as the study visit. Separately for men and women, we fit linear mixed-effects models[24] to examine changes in cognitive function over time with a specific assessment of the effect of an incident stroke on the rate of cognitive change. The models included random intercepts and time effects to accommodate correlation of cognitive measures within participants over time and to allow participant-specific rates of cognitive change. The models included a main effect of time and a time-varying incident stroke (binary) variable that indicated when and whether the participant experienced an incident stroke. An incident stroke-by-time interaction term was added to allow both the level and the rate of change in cognitive function to change after an incident stroke. Thus, the models provided measures of level and rate of change in cognitive function prior to and subsequent to an incident stroke.

Model A included baseline age and years of education, time-varying depressive symptoms (CES-D scores), time-varying incident stroke, time, and the incident stroke-by-time interaction term. Model B added time-varying systolic BP to Model A. We transformed the 3MSE outcome as the natural log of errors (101-3MSE) to improve normality. The WL outcome was normally distributed and met model assumptions. We fit linear mixed-effects models to the 3MSE and WL cognitive function responses. First, we tested the 3-way interaction of gender-by-incident stroke-by-time in models that included men and women. Then, we stratified our models on gender for three reasons. First, we had planned to assess effect modification of the stroke-cognitive function relationship by gender using

stratification *a priori*, regardless of the significance of the 3-way gender-by-incident stroke-by-time interaction term. Second, visual examination of participant-specific plots of cognitive function over time by gender suggested gender differences in the post-stroke trajectories of both the 3MSE and WL cognitive outcomes. Third, gender-stratified models provided measures of level and rate of change in cognitive function prior to and subsequent to an incident stroke within each gender group. We used routines in SAS version 9.2 (Research Triangle Institute, Research Triangle Park, NC) to fit all models and carry out all analyses.

Results

Subject Characteristics

We identified 151 adults (mean age, 72 ± 8 years) with incident first-ever stroke during ten years of follow-up. Among participants with incident stroke, the mean years of post-stroke follow-up for women was 3.6 years and 3.4 for men. Pre-stroke, the number of 3MSE tests was 3.7 in men and 3.8 in women. In the post-stroke period, there were 1.8 3MSE tests in men and 2.1 in women. The mean number of WL tests pre-stroke was 4.1 in men and 4.2 in women and 1.6 in men and 1.9 in women in the post-stroke period. None of these differences were significant.

The characteristics by gender among all participants and among those with first-ever stroke are presented in Table 1. Among all participants, prior to an incident stroke, women had fewer years of education, higher prevalence of anti-hypertensive medication use, higher depressive symptoms and higher WL scores compared with men. Men were more likely than women to be current smokers and to have coronary heart disease. At baseline, systolic BP and diastolic BP were lower in women compared with men.

Among participants with incident strokes, pre-stroke depressive symptoms and WL scores were higher in women compared with men; however, the pre-stroke percent with BP below 140/90 mm Hg was higher in men compared with women (58% vs. 42%; P=0.06). Following incident stroke, there were non-significant trends toward higher systolic BP and lower percent with BP below 140/90 mm Hg in women.

3MSE Errors by Gender

In unadjusted models of 3MSE in the overall study cohort, the 3-way interaction of gender-by-incident stroke-by-time was not significant (P=0.22)(data not shown). According to gender-stratified models, prior to occurrence of an incident stroke, 3MSE errors increased by 2.4%/year in men and increased by 3.3%/year in women (**Model A**, Table 2). Post-stroke changes in 3MSE errors were statistically significant in men and women. Post-stroke mean changes in 3MSE errors by gender from Model A are shown in the Figure. Within each gender-specific model, the incident stroke-by-time interaction term was significant. Over the post-stroke period, 3MSE errors increased by 22%/year (95% CI, 6.8%–36.7%) in men and 13.2%/year (95% CI, 3.5%–22.9%) in women. The trajectory of change in errors suggests a gender difference, although as previously noted, the gender-by-incident stroke-by-time interaction term was not significant.

Word List Scores by Gender

In unadjusted models of WL in the overall study cohort, the 3-way interaction of gender-by-incident stroke-by-time was not significant (P=0.42)(data not shown). According to gender-stratified models, prior to an incident stroke, WL scores improved by 0.3%/year in men (P=0.06) but worsened by 0.7%/year in women (P<0.001) (**Model A**, Table 2). Post-stroke changes in WL scores were not statistically significant in either gender. However, the magnitude of post-stroke change in WL scores was 1.7 times larger in women than in men. Post-stroke WL scores improved by 0.05 words/year (95% CI, −0.24–0.33) in men and by 0.09 words/year (95% CI, −0.16–0.34) in women. Post-stroke changes in WL scores were relatively constant over time in both men and women. Moreover, the magnitude of post-stroke change in the intercept showed a greater decrease in women (toward lower WL scores) compared with men.

Effect of Adjustment for Systolic Blood Pressure

Adjustment for time-varying systolic BP improved the model fit for all models (see values for -2logL in Table 2). Within each gender, significant post-stroke changes in 3MSE errors persisted after adjustment for time-varying systolic BP (**Model B**, Table 2). Time-varying systolic BP itself was not associated with the 3MSE errors in either gender. Time-varying systolic BP was not associated with WL scores in men (P=0.10) but higher systolic BP levels were associated with lower WL scores in women (P=0.002). However, in the WL models, adjustment for time-varying systolic BP had no effect on the associations between stroke and WL scores for either gender. A higher number of 3MSE errors and lower WL scores were associated with increasing age, fewer years of education, and more depressive symptoms in men and women (**Models A and B**, Table 2).

Discussion

In this population of older Mexican Americans, cognitive function declined post-stroke but did not differ significantly by gender. We observed dramatic declines in global cognitive scores (3MSE errors) after stroke in both women and men. We did not observe significant post-stroke differences in WL verbal memory scores for women or men. These findings persisted after adjustment for age, education, and time-varying depressive scores. We found no evidence that systolic BP influenced PSCD in either gender.

Our data indicate that 3MSE scores steadily worsened after stroke; whereas, WL scores worsened and then improved slightly over time. It is possible that the acute stroke injury caused executive dysfunction that improved or resolved with stroke recovery, changes reflected in the WL score trajectories and typical of vascular cognitive impairment. Furthermore, the acute stroke injury may have triggered progression of global cognitive dysfunction associated with early or latent Alzheimer's disease, changes reflected in the 3MSE scores. Previous data support this hypothesis.[11, 25, 26]

Few studies have assessed gender differences in post-stroke cognitive trajectories over prolonged time periods or in a population-based fashion.[12] A recent meta-analysis (n=24 studies) found that female gender was associated with increased odds of post-stroke

dementia (OR 1.3; 95% CI, 1.1–1.6) but there was significant heterogeneity between studies (P=0.004) and few Hispanics included.[2] Moreover, the pooled studies evaluated post-stroke dementia as the outcome, thereby making direct comparisons to our study of cognitive trajectories problematic.[2] For studying cognitive decline, continuous measures are most informative.[27] Our study highlights that PSCD is dynamic and variable, with trajectories changing over time post-stroke and differing by the cognitive test used to measure PSCD.

As shown in the recent meta-analysis,[2] the relationship between gender and post-stroke dementia is inconsistent across studies. While some research studies have found no gender differences in PSCD,[3, 4] other investigations have found rates of PSCD incidence to be higher in men[28] or higher in women.[29, 30] However, the studies that found women to have higher risk of incident dementia after stroke, one of which included Caribbean Hispanics, also showed that the risk was attenuated by socio-demographics, stroke features and clinical factors,[29, 30] findings consistent with other research.[2] Importantly, findings of gender differences in PSCD may depend on when PSCD is assessed after stroke and the ethnic group or geographic region in which it is assessed. In some ethnic groups or geographic regions, greater pre-stroke social isolation,[31] a predictor of incident stroke in women[32] and poor post-stroke outcomes,[33] may lead to worse PSCD in women early after stroke; whereas, subsequent social integration may promote cognitive resilience over time post-stroke.[34] Thus, study differences in population-level and patient-level characteristics (i.e., socio-demographics and clinical factors), methodology (i.e., the diagnostic criteria for PSCD), and the time interval between stroke and cognitive assessment potentially explain conflicting reports of gender variations in PSCD.[27]

While our findings may reflect no true association between gender and PSCD in older Mexican Americans, other potential explanations for our failure to find significant gender variations in PSCD also include insufficient sample size and differences in stroke case ascertainment or PSCD measurement. First, the sample size of incident strokes (n=151) may be inadequate to detect a significant association between the three-way interaction term (gender-by-incident stroke-by-time) and cognitive function. Second, stroke history was self-reported as a physician diagnosis and subject to recall bias and reporting error. However, recent data suggest high self-reported stroke accuracy including in the disabled elderly (sensitivity rates of 80–98%)[35, 36] with substantial reliability in minorities.[37] Lack of data on focal neurologic deficits or stroke features,[2, 4] neuroimaging,[38] and neuropathology may reduce our accurate selection of stroke cases. Although these data may improve the diagnosis of stroke and post-stroke dementia, they have not been shown to improve the performance of measures of pre-stroke and post-stroke cognitive function in estimating PSCD.[4] Third, we measured cognitive function using the 3MSE and WL tests at variable durations after stroke. This approach may be insensitive to detecting gender differences in PSCD. PSCD may affect cognitive domains, other than WL or 3MSE, and these may differ by gender.[19]

We found that, among women and men, adjustment for systolic BP 1) had no effect on the association between PSCD and cognitive performance; and 2) was weakly associated with lower verbal memory scores. Our results are consistent with research showing that elevated systolic BP is associated with cognitive decline only in the absence of stroke.[39] Although

previous research in Mexican Americans reported less control of hypertension in women compared with men,[14] we observed similar pre-stroke BP control (BP below 140/90 mm Hg) in women and men among all participants, and found non-significant trends toward less BP control in women compared with men among those with incident stroke before and after the stroke. With recent data[23] suggesting a hypertension-PSCD association, our findings of no association has three potential explanations: 1) our cognitive measures may not detect PSCD attributable to systolic BP; 2) age may modify the relationship between BP, CVD, and cognition[40]; and 3) pre-stroke effects of BP on cognition may supersede concurrent effects of BP on PSCD.

While this epidemiologic community-based study has less information for diagnosis and classification compared with clinical or hospital-based samples, it has fewer selection biases, more representative sampling and increased generalizability.[27] Still, results are generalizable only to non-institutionalized older Mexican Americans. Most attrition was due to death. We did not include recurrent stroke[11] in the models because this outcome was infrequent. Although we did not include anti-hypertension medication use in the models, we measured systolic BP and included it as a time-varying covariate. Although potential confounders such as stroke features, neuroimaging or neuropathology could bias our results if they differed by gender, we did not find significant gender differences in PSCD. Larger prospective studies with information on PSCD and sufficient sample size are needed to confirm our findings.

In this population of older Mexican Americans, 3MSE scores steadily worsened after stroke while WL scores worsened and then improved slightly over time. However, PSCD did not differ by gender. We found no evidence that systolic BP influenced PSCD in women or men.

Acknowledgments

Disclosures

Study Funding: Work on this manuscript was partially supported by NIH contracts AG12975 and DK60753.

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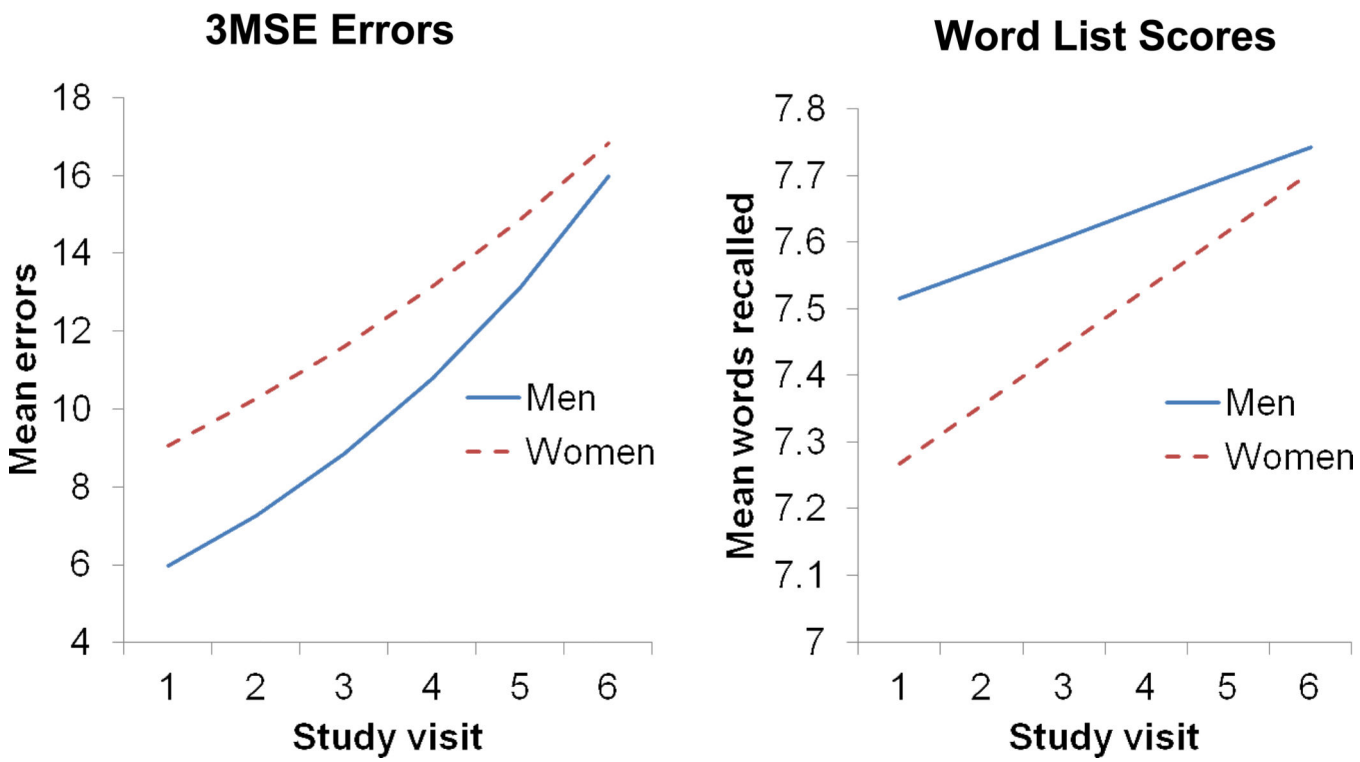

Figure 1.

Predicted Mean Post-stroke Cognitive Performance by Gender: The SALSA Study, 1998–2008

*Predicted mean cognitive performance scores were adjusted for enrollment age and education, and time-varying depressive scores.

J Stroke Cerebrovasc Dis. Author manuscript; available in PMC 2014 October 01.

Table 1

Characteristics of All Participants and Stroke Survivors by Gender: The SALSA Study, 1998–2008

	All Subjects			First-Ever Stroke Subjects		
Baseline Characteristics	**Men (n=655)**	**Women (n=921)**	**P**	**Men (n=66)**	**Women (n=85)**	**P**
Age, mean (SD), years	70.2 (6.7)	70.1 (6.9)	0.92	72.8 (8.1)	71.6 (7.8)	0.35
Age immediately before first stroke, mean (SD), years				76.0 (8.6)	74.7 (8.3)	0.33
Education, mean (SD), years	8.0 (5.6)	6.9 (5.1)	<0.001	7.6 (5.6)	7.0 (5.9)	0.54
Atrial fibrillation, % (N)	4.2% (27)	6.6% (59)	0.05	7.9% (5)	11.9% (10)	0.43
Diabetes, % (N)	33% (211)	30% (273)	0.23	43% (28)	40% (34)	0.70
Depressive symptom scores (CESD), mean (SD)	7.3 (8.7)	11.4 (11.2)	<0.001	8.8 (9.9)	13.5 (12.6)	0.03
Depressive symptom scores (CESD), mean average pre-stroke (SD)	7.6 (6.8)	11.5 (9.0)	<0.001	8.6 (7.6)	13.9 (10.8)	0.001
Use of anti-hypertensive medication, % (N)	5.5% (36)	11.0% (101)	<0.001	7.6% (5)	12.9% (11)	0.29
Recurrent stroke, % (N)	1.8% (12)	2.5% (23)	0.38	18% (12)	27% (23)	0.20
Current cigarette smoking, % (N)	16% (105)	7% (69)	<0.001	14% (9)	8% (7)	0.28
Coronary heart disease, % (N)	9.9% (64)	5.9% (54)	0.003	12.3% (8)	8.2% (7)	0.41
Congestive heart failure, % (N)	2.8% (18)	2.4% (22)	0.64	6.2% (4)	3.5% (3)	0.47
Systolic BP, mean (SD)	139.8 (19.2)	137.2 (19.2)	0.01	143.8 (23.0)	142.3 (19.0)	0.67
Diastolic BP, mean (SD)	78.0 (10.6)	74.5 (10.3)	<0.001	78.0 (9.6)	76.3 (10.3)	0.33
Systolic BP, mean average pre-stroke (SD)	140.4 (15.1)	139.5 (16.0)	0.25	142.8 (18.6)	144.5 (16.4)	0.55
Diastolic BP, mean average pre-stroke (SD)	77.0 (8.5)	75.3 (7.9)	<0.001	77.9 (9.0)	77.3 (8.1)	0.68
BP < 140/90, mean average pre-stroke (SD)	55% (360)	57% (528)	0.35	58% (38)	42% (36)	0.06
3MSE, mean (SD)	86.7 (10.0)	85.4 (12.1)	0.17	83.3 (12.1)	85.1 (11.8)	0.29
Word-List score, mean (SD)	7.8 (2.8)	9.2 (2.9)	<0.001	7.0 (2.9)	8.7 (3.0)	0.001
Post-stroke Characteristics						
Use of anti-hypertensive medication–at first visit post-stroke, % (N)	NA	NA	NA	16.7% (8)	25.4% (18)	0.26
Depressive symptom scores (CESD), mean average post-stroke (SD)	NA	NA	NA	13.2 (10.8)	15.8 (11.0)	0.23
Systolic BP, mean average post-stroke (SD)	NA	NA	NA	139.9 (20.8)	146.4 (17.7)	0.08
Diastolic BP, mean average post-stroke (SD)	NA	NA	NA	75.5 (9.4)	75.4 (8.8)	0.94
BP < 140/90, mean average post-stroke (SD)	NA	NA	NA	68.2% (45)	54.1% (46)	0.08

Table 2

Pre-stroke and Post-stroke Differences in Cognitive Scores by Gender from a Linear Mixed Effects Model: The SALSA Study, 1998–2008

3M5E Errors (Natural Log)				
	Model A		Model B	
Variable	**Men (n=646)**	**Women (n=912)**	**Men (n=615)**	**Women (n=861)**
-2 LogL	5812.2	8060.2	4965.5	6505.9
	Parameter (SE)	Parameter (SE)	Parameter (SE)	Parameter (SE)
Intercept	1.23 (0.26)§	0.99 (0.22)§	0.92 (0.27)§	0.85 (0.22)§
Pre-stroke change per visit	0.02 (0.008)‡	0.03 (0.007)§	0.003 (0.007)	0.005 (0.005)
Age, per year	0.02 (0.004)§	0.03 (0.003)§	0.02 (0.004)§	0.03 (0.003)§
Education, per year	−0.08 (0.004)§	−0.08 (0.004)§	−0.08 (0.004)§	−0.09 (0.004)§
Depressive symptom score, per point	0.006 (0.002)‡	0.003 (0.001)†	0.008 (0.002)§	0.005 (0.001)§
Systolic BP, per 10 mm Hg			0.01 (0.01)	0.002 (0.01)
Post-stroke intercept	0.60 (0.39)	0.71 (0.29)†	0.29 (0.38)	0.49 (0.28)
Post-stroke-by-time interaction term	0.17 (0.06)‡	0.09 (0.04)†	0.16 (0.06)‡	0.12 (0.04)‡
Post-stroke change per visit	0.20 (0.06)‡	0.12 (0.04)‡	0.17 (0.06)‡	0.13 (0.04)‡
Word-List Scores				
	Model A		**Model B**	
Variable	**Men (n=646)**	**Women (n=912)**	**Men (n=615)**	**Women (n=861)**
-2 LogL	11972.7	17844.3	11727.4	17426.8
	Parameter (SE)	Parameter (SE)	Parameter (SE)	Parameter (SE)
Intercept	14.30 (0.86)§	17.39 (0.75)§	14.73 (0.94)§	18.20 (0.80)§
Pre-stroke change per visit	0.04 (0.02)	−0.13 (0.02)§	0.04 (0.02)	−0.11 (0.02)§
Age, per year	−0.11 (0.01)§	−0.13 (0.01)§	−0.10 (0.01)§	−0.13 (0.01)§
Education, per year	0.14 (0.01)§	0.16 (0.01)§	0.14 (0.01)§	0.15 (0.01)§
Depressive symptom score, per point	−0.02 (0.006)§	−0.02 (0.004)§	−0.02 (0.006)§	−0.02 (0.004)§
Systolic BP, per 10 mm Hg			−0.04 (0.02)	−0.06 (0.02)‡
Post-stroke intercept	13.98 (1.07)§	15.63 (0.92)§	14.41 (1.14)§	16.45 (0.97)§
Post-stroke-by-time interaction term	0.003 (0.15)	0.21 (0.13)	0.003 (0.15)	0.20 (0.13)
Post-stroke change per visit	0.05 (0.15)	0.09 (0.13)	0.05 (0.15)	0.09 (0.13)

Estimate (Standard Error):

†P≤0.05;

‡P≤0.01;

§P≤0.001.

Model A included baseline age and years of education, time-varying depressive symptoms (CES-D scores), time-varying incident stroke, time, and the incident stroke-by-time interaction term. Model B added time-varying systolic BP to Model A.